#9 RW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICANT	: Jackowski *et al.*
INVENTION	: **Protein Biopolymer Markers Indicative of Insulin Resistance**
SERIAL NUMBER	: 09/993,392
FILING DATE	: November 23, 2001
EXAMINER	: Cheu, C. Jacob
GROUP ART UNIT	: 1641
OUR FILE NO.	: 2132.097

CERTIFICATE UNDER 37 CFR 1.8(a)
I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 on 9-16-2003

Mail Stop: Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 CFR § 1.132

I, Dr. George Jackowski, do hereby declare as follows:

1. I am Chief Executive Officer and Chief Science Officer of Syn-x Pharma Inc., assignee in the application entitled **"Protein Biopolymer Markers Indicative Of Insulin Resistance"**, having U.S. Application Serial No. 09/993,392, filed November 23, 2001.

2. In the Office Action mailed on April 23, 2003, claims 10-28 (as originally presented) were rejected under 35 U.S.C. 112, first paragraph because the claimed invention allegedly contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with

which it is most nearly connected, to make and/or use the invention. The Examiner states that the invention is directed to identification of a particular disease, for example, insulin resistance, by determining the presence of certain biopolymer markers in a sample, such as peptides selected from the group consisting of amino acid residues 2-11 of SEQ ID NO:1; amino acid residues 2-12 of SEQ ID NO:2 and amino acid residues 2-13 of SEQ ID NO:3. The Examiner asserts that the experiments disclosed in the specification do not sufficiently support that the claimed peptides are biopolymer markers of insulin resistance disease. The Examiner is particularly concerned with an alleged lack of controls in the experiments.

3. This declaration is submitted in order to clarify the use of controls in the experiments disclosed in the specification.

4. There are no conventional controls applied in the methods of the instant invention. Both samples from diseased patients and samples from healthy patients are separated by polyacrylamide gel electrophoresis. The gel is then examined in order to identify differences in the bands appearing in diseased and healthy patients. The bands, which differ between healthy and diseased patients, are excised and purified from the gel. A determination of upregulation, downregulation, presence and/or absence of the proteins present in the bands is assessed by sample wherein they appear, for example, the claimed peptide fragments were identified and excised from bands which appeared in the diseased samples, thus this can be considered to be upregulation of the protein in the

disease sample as compared to the absence of the protein in the healthy sample. This comparison between two physiological states as evidenced by the bands appearing on the gel represents an inherent control in the experiment. The claimed protein fragments excised from the band appearing in the diseased sample are sequenced and identified through the application of mass spectrometric techniques. Since no corresponding band appeared in the healthy sample, there is no identification of normal protein fragments, thus a comparison of mass spectra from diseased and healthy patients is not necessary in these experiments. It is standard laboratory practice to sequence peptides by mass spectrometry and identify the peptides based upon known sequences available in databases; thus sequencing and comparison of control peptides is not required. One of ordinary skill in the art would be familiar with these standard protocols of mass spectrometry.

The undersigned declares that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the Application or any patent issuing thereon.

Sept 15 2003
Date

George Jackowski